Cardiovascular risk assessment in low-resource settings

Original Article

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Cardiovascular risk assessment in low-resource settings: a consensus document of the European Society of Hypertension Working Group on Hypertension and Cardiovascular Risk in Low Resource Settings

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The Global Burden of Diseases, Injuries, and Risk Factors Study 2010 confirms ischemic heart disease and stroke as the leading cause of death and that hypertension is the main associated risk factor worldwide. How best to respond to the rising prevalence of hypertension in resource-deprived settings is a topic of ongoing public-health debate and discussion. In low-income and middle-income countries, socioeconomic inequality and cultural factors play a role both in the development of risk factors and in the access to care. In Europe, cultural barriers and poor communication between health systems and migrants may limit migrants from receiving appropriate prevention, diagnosis, and treatment. To use more efficiently resources available and to make treatment cost-effective at the patient level, cardiovascular risk approach is now recommended. In 2011, The European Society of Hypertension established a Working Group on 'Hypertension and Cardiovascular risk in low resource settings', which brought together cardiologists, diabetologists, nephrologists, clinical trialists, epidemiologists, economists, and other stakeholders to review current strategies for cardiovascular risk assessment in population studies in low-income and middle-income countries, their limitations, possible improvements, and future interests in screening programs. This report summarizes current evidence and presents highlights of unmet needs.

Keywords: cardiovascular risk, global cardiovascular and cerebrovascular health, low-income and middle-income countries, migrants and minority groups

Abbreviations: ACR, albuminuria to creatininuria ratio; CKD, chronic kidney disease; CVD, cardiovascular disease; ESH, European Society of Hypertension; GBD, Global Burden of Disease; LMIC, low-income and middle-income countries; STEPS, STEPwise Approach to Stroke Surveillance

HYPERTENSION IN A GLOBAL PERSPECTIVE

According to the Global Burden of Disease (GBD) 2010 study, the most comprehensive and comparable assessment of mortality and loss of health to date [1], cardiovascular disease (CVD) is the leading cause of death worldwide, 80% of the 16.7 million deaths due to CVD occur in low-income and middle-income countries (LMICs) and hypertension is now the leading associated

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risk factor [1,2]. High blood pressure (BP) accounts for 9.4 million (95% UI 8.6 million to 10.1 million) deaths and 7.0% (6.2–7.7) of global disability-adjusted life years (DALYs), more than elevated BMI, fasting plasma glucose, and total cholesterol combined [2].

As of 2008, almost 1 billion people have uncontrolled hypertension worldwide [3]. The African region has the highest prevalence rate, 46% of adults aged 25 and above, whereas the Americas have the lowest prevalence, at 35%. In contrast with other CVD risks such as high BMI, the burden of hypertension is greater in lower income countries than higher income settings [3,4]. In an urban African setting, the stroke death rate (a proxy of hypertension prevalence and control) was reported to be five-fold higher than that in England [5,6]. According to WHO data, age-standardized death rate (per 100 000 population) is 141 in the African region and 93 in the European region [7]. Multiple risk factors positively interact to exacerbate CVD risks. Hypertension, for example, combined with unhealthy diets and lack of physical activity (sodium and alcohol consumption, high BMI, and low physical activity), has a multiplicative negative effect on CVD mortality and DALYs [2]. A substantial part of the CVD risk of death and DALYs attributable to these factors is not also exacerbated by, but also mediated through high BP [2]. In LMICs, overweight or obesity was associated with hypertension [8–11] or progression to hypertension [12]. Cultural aspects can also increase or decrease exposure to risk factors. The odds of obesity in LMICs is especially high for women [13], particularly in the Middle East and North Africa [14]. Sex differences for abdominal obesity start at early adolescence [15], probably due both to a preferred body image [16–18] and to food insecurity [19–22]. Education and socioeconomic inequality seem to play a role in the development of obesity [23] as well as in the access to care for hypertension [10,24–30], especially in women. Sex association of obesity in adulthood was indeed lost after accounting for education and socioeconomic factors [20,31].

Hypertension is also a determinant of chronic kidney disease (CKD), a recognized marker of the poor health outcomes of hypertension and diabetes [32]. However, growing evidence indicates that CKD is a strong cardiovascular risk factor in itself [32]. Other causes of CKD in LMICs will be discussed later on in this article. In the general population, glomerular filtration rates (GFRs) lower than 60 ml/min/1.73 m^2 and albuminuria (one of the earliest manifestations of CKD) were found to be associated with an independent risk of cardiovascular morbidity and mortality [33–36]. The fact that milder CKD affects 5–7% of the world population and is more common in LMICs and in disadvantaged and minority populations is worth noting [37,38]. Taken together, these findings underline the add-on role of CKD to the common recognized risk factors for global and cardiovascular mortality.

How best to respond to the rising prevalence of hypertension in resource-deprived settings is a topic of ongoing public-health debate and discussion. On the one hand, according to the Disease Control Priorities Project, two prevention strategies at population level, salt reduction and tobacco control, and a multidrug strategy to treat patients with high-risk CVD meet the condition of cost-effectiveness multiple interventions in LMICs [39,40]. Population strategies supported by communication media with the concerted action of local authorities might induce cultural changes and the adoption of healthy lifestyle. On the other hand, WHO recommends identification of individuals with high-risk CVD in LMICs to make cost-effective the allocation of available resources. Cardiovascular risk stratification might, however, require facilities not easily available in LMICs. In 2011, the European Society of Hypertension established a Working Group on 'Hypertension and Cardiovascular risk in low resource settings', which brought together cardiologists, diabetologists, nephrologists, clinical trialists, and other stakeholders to review current strategies for cardiovascular risk assessment in population studies, their limitations, possible improvements, and future interests in screening programs. This report summarizes current evidence from the Working Group and presents highlights of unmet needs for intervention and research at patient and population levels.

PREVENTION STRATEGIES AT POPULATION LEVEL

High sodium intake has effects on BP [41–43], all-cause mortality, CVD, stroke, and coronary heart disease, which have been recently quantified by the WHO Nutrition Guidance Expert Advisory Group Subgroup on Diet and Health [44–46]. When sodium intake was less than 2 g/day, SBP was reduced by 3.47 mmHg (0.76–6.18) and DBP by 1.81 mmHg (0.54– 3.08) as compared to a sodium intake $\geq$ 2 g/day. Increased sodium intake was associated with an increased risk of stroke (risk ratio 1.24, 95% confidence interval 1.08–1.43), stroke mortality (1.63, 1.27–2.10), and coronary heart disease mortality (1.32, 1.13–1.53) [47]. Estimation of the effects of low-sodium vs. high-sodium intake on BP showed a greater increase in hypertensive and black populations than in normotensive individuals and whites, respectively [48]. The 2002 joint World Health Organization/Food and Agriculture Organization of the United Nations expert consultation [49] and the 2007 WHO guideline [50] recommend a sodium intake not greater than 2 g/day . In LMICs, tobacco consumption is increasing by 3.4% per year and smoking rates are also increasing [51,52]. In developed countries, 35% of men and 22% of women smoke, whereas in LMICs, 50% of men and 9% of women are smokers. A favorable association between smoking cessation and BP decrease over time and risk to develop hypertension in an adult sample of generally healthy men has recently been reported [53]. More than 50% of world's population now lives in urban areas where sodium consumption and tobacco use are consistently high [28,54]. Mass media campaigns have a direct impact on populations, but are expensive and require the support of local health authorities. An increasing proportion of governments in western countries have moved to ban all promotion of cigarettes and smoking via the electronic and print media [55]. Involvement of mass media-newspapers, magazines, radio, television, and films may change cultural models and help in adopting healthy lifestyle by young people. James Bond had his last cigarette in 1989 in '*Licence to kill*', but still drinks. Exposure to alcohol advertising

is strongly associated with the likelihood of adolescents starting to drink [56,57], as well as with increased alcohol consumption among young people [58,59]. Alcohol consumption increases BP values both in hypertensive and normotensive individuals [60–62]. Attention should also probably be paid on sugar in foods and beverages, an independent risk factor in LMICs for the metabolic syndrome [63].

TREATMENT STRATEGY AT THE PATIENT LEVEL

The multidrug strategy to treat patients with high cardiovascular risk also meets criteria for cost-effectiveness [39,40,64,65], and WHO fully recognizes the paradigm shift from the treatment of the single risk factor in isolation to the management of total cardiovascular risk [50,66]. Identification of patients with high-risk CVD is, thus, essential.

Cardiovascular risk stratification in low-income and middle-income countries

The first limiting factor is that facilities required to assess biochemical parameters for cardiovascular risk stratification may not be easily available in LMICs. Therefore, cardiovascular risk stratification packages proposed in 2002 by WHO were based on history, BP measurement, and selective urine analysis (performed only if BP $\geq$140 or $\geq$90 mmHg) [67]. More precisely, the WHO CVD-Risk Management Package considered three different scenarios (nonphysician health worker; medical doctor or specially trained nurse; medical doctor with access to full specialist care; Table 1) [68]. The second limitation is that most of available equations developed to predict individual absolute risk of a cardiovascular event over a specified time period [69–76] were derived from European descent populations in high-income countries and are not necessarily valid in other populations [75,77]. Therefore, WHO/International Society of Hypertension (ISH) produced specific risk prediction charts [50] using population-based standardized collection and assessment of data on risk factor prevalence and relative risk (heart attacks and stroke). Data were obtained in WHO epidemiologic subregion survey from the Comparative Risk Assessment Project [54], and in the Asia Pacific Cohort Studies Collaboration [78–82]. These charts have the same goal as existing risk equations such as those based on Framingham and SCORE [69,72]. Absolute risk of cardiovascular events was determined by scaling individual relative risk to population incidence rates of major CVDs, estimated from the GBD study [50,65,66]. WHO/ISH charts enable cardiovascular risk assessment and prediction in LMIC populations of all WHO subregions on the basis of age, sex, SBP, type 2 diabetes mellitus, smoking status, and total serum cholesterol [50,66]. Detection of abnormalities of glucose metabolism such as impaired glucose tolerance, or the 'metabolic syndrome' is worthwhile, because some diabetes could be prevented by focused intervention on lifestyle. Screening for diabetes is more cost-effective for people in the hypertensive and obese subgroups, the costs of screening being offset in many groups by lower future treatment costs [83]. A third potential limitation is that easy obesity measurements (BMI or waist circumferences) are not included in the WHO/ISH charts, although there is strong evidence of the importance of obesity to guide intervention strategies aimed at reducing the incidence of type 2 diabetes. The global rise in overweight and obesity suggests that health promotion interventions at population level have not so far been effective, but improving lifestyles and increasing exercise in high-risk individuals remains a crucial issue. Therefore to include waist circumferences in the risk assessment could enhance awareness. Assessment of proteinuria is also not included in WHO charts, although recognizing that CVD risk may be higher than indicated in the chart in people with proteinuria.

Implementation of cardiovascular risk strategies and WHO/ISH Risk prediction charts in LMICs has different implications. First, this approach restricts unnecessary drug treatment to low-risk patients [84]. This point is especially important in LMICs where much of the costs of healthcare are currently shifted directly to patients. The WHO estimates that out of pocket expenditure of more than 15–20% can lead to impoverishment; India's proportion in 2010 was 61% [85]. Achievement of universal health coverage is a crucial step for sustainable development and for reducing poverty and social inequality, and currently represents a global goal of 'Health for all as a human right' [86]. Implementation of cardiovascular risk strategies in this context might, thus, provide a way to use limited resources more efficiently [87]. Second, the threshold of cardiovascular risk for deciding the start of drug treatment can be adjusted to suit the country context. Cost-effectiveness of an intervention indeed depends on the gross domestic product per head for the country. WHO proposed different 10-year total CVD risk thresholds for intensive intervention based on countries resource level (20% for high-resource setting; 30% for medium-resource setting; 40% for low-resource setting). Third, a little conflict with the main content may, however, exist because although cardiovascular risk stratification might be especially important for health systems of countries with very limited resources, the screening or identification of those with very high risk from the population may be much more expensive than treating only

TABLE 1. Characteristics of the three scenarios in the WHO CVD-Risk Management Package

Resource availability	Scenario 1	Scenario 2	Scenario 3
Human resources	Nonphysician health worker	Medical doctor or specially trained nurse	Medical doctor with access to full specialist care
Equipment	Stethoscope, blood pressure measurement device, measuring tape or weighing scale; Optional: test tubes, holder, burner, solution or test strips for checking urine glucose	Stethoscope, blood pressure measurement device, measuring tape or weighing scale; Test tubes, holder, burner, solution or test strips for checking urine glucose and albumin	Stethoscope, blood pressure measurement device, measuring tape or weighing scale, electrocardiograph, ophthalmoscope, urine analysis, blood analysis: fasting blood sugar, electrolytes, creatinine, cholesterol and lipoproteins

Data from [68].

hypertension. In many LMICs, facilities available for cholesterol assay are limited, although it is often feasible to check urine sugar as a surrogate measure for diabetes. In this regard, WHO/ISH charts have a second version, for use where measurement of cholesterol level is not possible [50]. If the resources are really limited, it is a preferred strategy to work only on hypertension and smoking and not on lipid and diabetes because a lower risk is attributed to them.

Despite drugs being a major contributor to healthcare costs, Mendis *et al.* [84] found that reducing the cardiovascular risk threshold for drug treatment from 30 to 20% in LMIC populations did not substantially increase the cost of treatment. Moreover, as the cardiovascular risk threshold for drug treatment is lowered, there is a concomitant increase in health benefits [67].

Cardiovascular risk assessment in population surveys

When performing population surveys in LMICs, a door-to-door approach has different advantages: data collected with a door-to-door approach allow avoiding the selection bias affecting hospital data in LMICs where universal health coverage is uncommon; the use of point-of-care instruments for biochemical assays of blood glucose and lipids, the procedure suggested by WHO, limits pre-analytical errors (storage, transportation, standardization of procedure) [88]. WHO recommends the use of affordable and reliable electronic devices for BP measurement that have the option to select manual readings [89–91]. Cost of personnel is a main component of budget in population surveys. Personnel costs and the logistic difficulties connected with organizing a two-visit strategy, therefore, lead to the adoption of a single-visit strategy in the WHO STEPwise Approach to Stroke Surveillance [92] (STEPS) aimed at assessing cardiovascular risk in populations. Although the program allows structured between countries comparison and within country follow-up of implementation of prevention strategies, its results cannot be directly transferred to cost estimation for the plan of prevention strategies. High BP is the main factor guiding cardiovascular risk stratification and the diagnosis of hypertension requires recording BP values for several days in repeated visits [93–95]. When the estimation of hypertension prevalence based on two visits was compared with the estimation based on a single visit, the strategy adopted in the STEP program, hypertension prevalence reduced by 12% in a cohort of individuals aged 62 ± 11 years [96], by 35% in a cohort of individuals aged 39 ± 9 years [97], and by 35% in a national wide survey for the age range between 15 and 69 years (Fig. 1) [98]. Differently from what was expected, misclassification is more common at young ages, two-thirds of men less than 30 years of age having normal BP values at the second visit [98]. Thus, screening an individual at high cardiovascular risk at the first visit is crucial, but the panel of tests that can be included in surveys is to be seen in the perspective of costs. It is indeed unreliable to perform an echocardiogram in all participants in a national survey. However, the inclusion of a urine dipstick test for proteinuria in the test panel might be a sustainable approach. Proteinuria allows classifying a patient in the high or very high class of 10-year risk of cardiovascular mortality as defined by international guidelines for the management of hypertension [93–95,99,100]. When urine dipstick for proteinuria was added to the parameters included in a national survey based on two-visit assessments [98], the prevalence of individuals classified as at high or very high cardiovascular risk at the first visit remained stable at the second visit. More precisely, only 1.9% of individuals classified as at high or very high cardiovascular risk at the first visit moved to average, low or moderate cardiovascular risk categories at the second visit [98]. With this approach, a stable estimation of individuals at high cardiovascular risk could be obtained already at the first visit.

Implications for chronic kidney disease assessment in low-income and middle-income countries

In western countries, the current debated question is 'who should be screened to make cost-effective urine dipstick for proteinuria?'. Diabetes and hypertension are the leading causes of CKD in all developed and in many developing countries [32], so that current trend is to perform a 'selective screening' [101,102]. WHO suggests performing urine dipstick test only if clinic BP is at least 140 or at least 90 mmHg, and dipstick test for proteinuria is not included in the WHO STEP program. However, risk factors may differ in other areas of the world [103,104] because glomerulonephritis and renal diseases of unknown causes are common in Asia

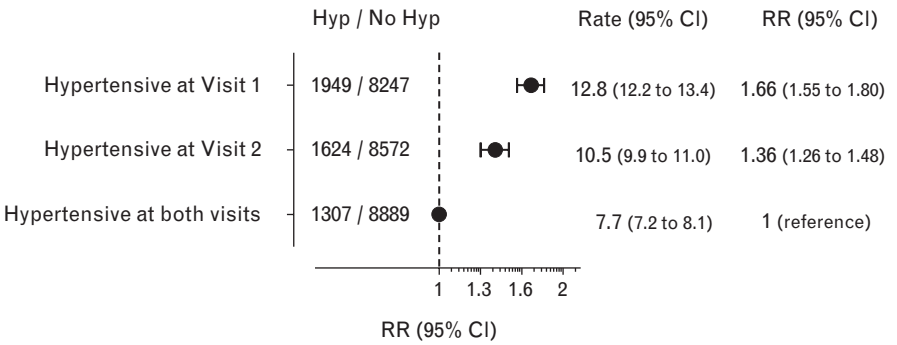

FIGURE 1 Diagnosis of hypertension (SBP $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mm Hg and/or self-reported use of antihypertensive drugs at the time of the interview) performed on the basis of measurements taken at the first visit (visit 1), at the second visit (visit 2), or both. The number of individuals with and without the condition and age-weighted rates are reported [98]. CI, confidence interval.

and sub-Saharan African countries [105]. In China, where the prevalence of proteinuria is high [106], glomerulonephritis, mainly postinfectious, is the main cause of CKD [105] and end-stage kidney disease [107–109]. Nephrotoxic effects can also result from consumption of potentially toxic herbs, incorrect substitution of harmless herbs with toxic herbs, contamination with toxic compounds, such as heavy metals, or interactions between herbs and conventional treatments [105,107,110,111]. The use of khat in Yemen was importantly associated with kidney damage (proteinuria $\geq +1$) after adjustment for several possible confounders (including hypertension and diabetes) [112]. Data collected from Nepal, Bolivia [113], and Yemen [10,112] showed that more than 5% of people younger than 60 years without previous history of diabetes and hypertension had microalbuminuria or proteinuria (Fig. 2, Table 2) [112,113]. On these bases, the Asian Forum of Chronic Kidney Disease Initiative recently suggested the addition of region-specific high-risk groups for screening, such as people exposed to harmful herbal preparations [111] or environmental factors [114]. In the absence of prospective studies performed in LMICs, it is impossible to infer that proteinuria, on a completely different background, should carry the same risk found in studies performed in industrialized societies. Likewise, although evidence for the benefits of CKD treatment with angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in patients with albuminuria combined with diabetes or CVD is strong in high-income countries [115], no randomized clinical trials have been performed in LMICs. However, integration of the urine dipstick test in screening surveys opens a perspective for sustainable cardiovascular risk assessment, and may increase health awareness in countries without advanced health systems [116]. The approach could be adapted to the conditions and socioeconomic circumstances of each nation [110].

The existing Manichean dualism of communicable and noncommunicable disease might lead physicians and researchers to disregard the evidence that some communicable diseases of children are the cause of cardiovascular events in adulthood. Rheumatic heart disease (RHD) is still causing most of the cardiovascular morbidity and mortality in young people in different world areas [117,118]. In China, RHD is a not negligible cause of atrial fibrillation and stroke [119–121]. If RHD is detected early, monthly penicillin injections (secondary prevention) are a cost-effective means of preventing more advanced, debilitating cardiac disease [122]. Costs make stethoscope an essential equipment in cardiovascular risk stratification (Table 1), although screening programs including primary echocardiography revealed prevalence rates up to 10 times higher than those resulting from clinical examination alone [123–126]. In February 2012, the World Heart Federation published the first evidence-based criteria for echocardiographic diagnosis of RHD, and removed clinical examination from the diagnosis [127]. Ultraportable, hand-held, pocket-sized imaging devices capable of producing two-dimensional and color images are now available [128], but in LMICs, physicians and expert sonographers are scarce. The possibility that low-cost electronic stethoscope able to reach a provisional diagnosis of cardiac valve disease might be developed to screen heart murmurs in children [129] is a sector of high potential interest [130]. These devices might be accessible to unskilled personnel for screening purposes.

NEW VULNERABLE/HIGH-RISK GROUPS IN EUROPEAN UNION COUNTRIES: IMPLICATIONS FOR HEALTH SYSTEMS

In 2010, 9.4% of the total European Union populations were foreign-born [131]. Age-standardized and sex-specific stroke mortality rates in Great Britain for 1979–1983, 1989–1993, and 1999–2003 were higher for all migrant groups in each time period compared with men born in England and Wales, men born in West Africa or Bangladesh, and women from Jamaica having the highest rates. More precisely in 1999–2003, stroke mortality was almost 200% higher among male migrants from West Africa, and almost 100% higher among those from the Caribbean [132]. These findings bear similarities with the high stroke

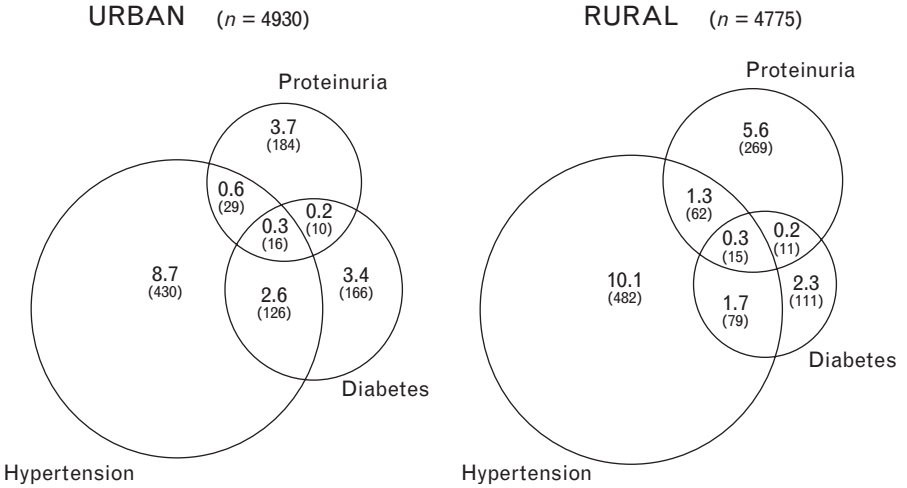

FIGURE 2 Venn diagram showing the amount of overlap between hypertension, diabetes, and proteinuria separately for the individuals from the urban ($n = 4390$) and rural area ($n = 4775$). Data are expressed as percentage of urban or rural individuals, the absolute number being reported in brackets [112].

TABLE 2. Prevalence of microalbuminuria proteinuria (≥1+ at dipstick test) in participants by country

Country	ACR (ACR>30 mg/g)			Proteinuria (≥1+ at dipstick test)			Reference
	All	Women	Men	All	Women	Men	
Nepal	7.8	7.1	8.8	3.5	3.3	3.8	[113]
Bolivia	–	–	–	4.5	4.0	5.5	[113]
Georgia	–	–	–	14.0	11.6	21.5	[113]
Yemen	–	–	–	6.2	5.3	7.0	[112]
USA	10.2	11.3	9.0	–	–	–	[113]

ACR, albuminuria to creatininuria ratio.

mortality of Surinamese and Antillean-born residents in the Netherlands [133]. There is consensus that among people of African origin, hypertension is three-fold to four-fold more prevalent than the native European population [75,134–139]. With few exceptions, incidence and prevalence of diabetes mellitus are also much higher among migrants than among locally born residents [11,137,140,141]. In the UK, the incidence of end-stage renal failure among individuals from ethnic communities is three to five times greater than among the native population [142,143]. Should these data be confirmed in the different European countries, a future burden of cardiovascular (myocardial infarction and stroke) and renal disease (dialysis) can be expected in the next few decades with relevant implications in terms of costs for health systems of European Union member countries.

European Union recognized the need to improve data collection on migrants' health aimed at the creation of specific prevention policies. However, many of the European Union programs have relied on the self-report of pathological conditions. This approach was useful to limit the costs of surveys, but sound data can only be obtained by directly assessing risk factors with the adoption of standardized forms to make results comparable between countries.

Migrants from LMICs usually develop cardiovascular complications in the medium-to-long term as a consequence of different environmental circumstances [77,144–147]. Cultural adaptations have great influence on the effectiveness of interventions among specific populations [148–150]. Therefore, intervention should not be focused only on the individual, but rather on the context and community; otherwise change may not be sustainable [151].

Policy initiatives should, thus, improve data collection, to adapt organization of health systems to cultures, and to provide information to migrants on health problems and services. Europe as a whole is often perceived as a group of wealthy countries where inclusive social protection systems provide comprehensive protection for the most vulnerable [154–156]. However, in times of financial constraint, policy discussions often circle around cutting back social protection expenditures. Only four European Union member states (Netherlands, France, Portugal, and Spain) offered undocumented migrants access to primary care [131,152,153], but recent reductions in health expenditures pose severe threats and lead to decisions limiting healthcare to migrants without sufficiently investigating the impacts on those in need [153]. A reduction in access to primary and specialist care is indeed unlikely to be cost-effective, as use of emergency services will increase [157,158]. Current budget restrictions may also widen health inequalities, hurting other population groups in the dominant ethnic groups (lower socioeconomic groups, the unemployed who comprise a very large group in Europe at present, those with limited education, and people with mental health issues) [159]. The drive to cost-effectiveness should, thus, be coupled with seeing health as an investment, avoiding myopic short-term savings through arbitrary healthcare cuts.

CONCLUSION

The clinical and epidemiological importance of CVD and high BP in LMICs markedly increased during the last decades and high BP is the leading risk factor. The establishment of culture of prevention in most LMICs requires the concerted action of television, radio, mass media-newspapers, and magazines, with the support of local health ministries and regulatory agencies, to limit salt intake and tobacco use.

Cost-effectiveness of prevention treatments at the patient level requires a cardiovascular risk approach. Identification of patients with high-risk CVD may indeed restrict unnecessary drug treatment to low-risk patients. The adoption of a cardiovascular risk approach in population surveys has also relevant implications for healthcare resource allocation decision-making. However, in low-resource settings, the screening or identification of those with very high risk from the population may be much more expensive than treating only hypertension. According to current evidence, some crucial points have to be considered both in surveys and patient care:

1. Hospital-based surveys have relevant selection bias, universal health coverage being uncommon in LMICs, so that a door-to-door approach is to be preferred;
2. Assessment of hypertension burden on the basis of a single visit may lead to overestimation of prevalence and healthcare requirements; thus survey strategies aimed at assessing global cardiovascular risk have to be considered;
3. Treatment gap is to be based on cardiovascular risk stratification (untreated individuals at high cardiovascular risk), rather than focusing on the single risk factors (untreated hypertensive patients);

4. Integration of urine dipstick test with cardiovascular health programs enhances the value of screening strategies;
5. Proteinuria and CKD in LMICs may result from post-infectious glomerulonephritis, or nephrotoxic agents so that the value of selective screening (diabetes and hypertension), currently adopted in high-income countries, might be limited in LMICs;
6. RHD still causes most of the cardiovascular morbidity and mortality in LMICs, so that the development of new strategies for optimization of the use of currently available devices (ultrasound), or the development of new low-cost device accessible to unskilled personnel to screen heart murmurs in children is a sector of high potential interest;
7. Global changes may have relevant implications for health systems of European countries, surveys exploring cardiovascular risk being now essential to focus prevention strategies in the setting of migrants and underserved communities living in Europe;
8. Intervention in the setting of migrants should not be focused only on the individual but rather on the context and community; otherwise change may not be sustainable.

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Conflicts of interest

There are no conflicts of interest.

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Reviewer's Summary Evaluation

Reviewer 1

This is an interesting summary of a huge body of work and should be of interest to readers who missed the main issue of the Lancet dealing with the Global Burden of Disease early in 2013. The main limitation is that it is not novel, but it does provide an interesting European perspective.